

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CP/58.689	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR97/01295	International filing date ( <i>day/month/year</i> ) 11 July 1997 (11.07.1997)	Priority date ( <i>day/month/year</i> ) 12 July 1996 (12.07.1996)
International Patent Classification (IPC) or national classification and IPC C12N 15/31, C07K 14/22, 16/12, A61K 39/095, C12Q 1/68, G01N 33/53		
Applicant INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE M		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 09 February 1998 (09.02.1998)	Date of completion of this report 10 November 1998 (10.11.1998)
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR97/01295

## I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

- ☐ the international application as originally filed.
- ☒ the description, pages 1-131, as originally filed,  
pages \_\_\_\_\_, filed with the demand,  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims, Nos. 1-32, as originally filed,  
Nos. \_\_\_\_\_, as amended under Article 19,  
Nos. \_\_\_\_\_, filed with the demand,  
Nos. \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
Nos. \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the drawings, sheets/fig 1/9-9/9, as originally filed,  
sheets/fig \_\_\_\_\_, filed with the demand,  
sheets/fig \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
sheets/fig \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

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## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	3-10, 12-14, 16-20, 22-23, 25, 28-32	YES
	Claims	1, 2, 11, 15, 21, 24, 26, 27	NO
Inventive step (IS)	Claims	3-10, 12-14, 16-20, 22, 25	YES
	Claims	1, 2, 11, 15, 21, 23, 24; 26-32	NO
Industrial applicability (IA)	Claims	1-32	YES
	Claims		NO

## 2. Citations and explanations

Reference is made to the following documents:

D1: Wolff et al., FEMS Microbiol. Lett., 125(2-3), pp.255-63, 1995

D2: Zhou et al., Mol. Microbiol., 6(15), pp.2135-46, 1992

D4: Strathdee et al., Gene, 166, pp.105-110, 1995

D5: WO 94/05703

D6: Devi et al., P.N.A.S., 88(16), pp.7175-79, 1991.

I) From a grammatical point of view, the wording used in claim 1 "...all or part of genes to be found in..." can be interpreted in two different ways (see first paragraph of VIII).

It may refer equally to (i) parts of **genes** to be found (présents) in *Neisseria meningitidis* but not in another bacterium (i.e. parts of genes, said genes to be found (présents in *Neisseria meningitidis* but not in another bacterium) and to (ii) **parts** of genes to be found (présentes) in *Neisseria Meningitidis* but not in a different bacterium.

Consequently, document D2 which describes **parts** of

genes to be found (*présentes*) in *Neisseria meningitidis* but not in *Neisseria gonorrhoeae*, in particular parts corresponding to the sequences 296 to 497 and 803 to 833 of the gene *argF* (see page 2139, right-hand column, first paragraph) anticipates the novelty of claims 1, 2, 15 and 21.

Document D1, which describes **parts** of genes (sequences derived from coding segments of the gene *Rmp*) to be found (*présentes*) in *Neisseiria meningitidis* and *Neisseria gonorrhoeae* but not in *Neisseria lactamica* (see Table 1, Fig.1 and page 258, right-hand column, second paragraph), destroys the novelty of claims 1, 11, 15 and 21.

II) The subject matter of claims 23 and 28 to 32 consists of common products and methods which do not involve an inventive step *per se* (see for example D5, in particular the claims and D6). Thus, since it refers to non-novel and non-inventive subject matter (such as that of claims 1, 2, 11, 15 and 21), no inventive step can be acknowledged therein (PCT Article 33(3)).

III) Although the wording "*Neisseria meningitidis*-specific DNAs" lacks clarity since a specific feature is, in principle, defined in relation to a reference system, this wording appears to be intended to designate, according to the applicant's own definition, "the nucleotide sequences which are only hybridized with those of *Neisseria meningitidis*" (see description of the application, page 7, lines 15 to 19).

Document D4 describes a method for obtaining *Neisseiria meningitidis*-specific DNA banks (see in

particular Fig.1 and the text relating thereto on page 106) comprising the three steps indicated in claim 24.

Even though the sequences obtained by the method described in D4 are specific to the *Neisseria meningitidis* genome ET15, they correspond to this definition.

D4 therefore anticipates the subject matter of claim 24.

Consequently, the products obtained by the method described in D4 form part of claim 26, where this claim refers to claim 24.

The subject matter of claim 26 is not therefore novel.

The subject matter of claim 27, which refers explicitly to the variants of a single species of cells, is also anticipated by D4.

- IV) The method described in claim 25 is novel and appears to involve an inventive step (PCT Article 33(2) and (3)), given the step whereby "chromosomal DNA is cut at random from the subtraction strain". This step avoids the contamination of the bank specific to *Neisseria Meningitidis* as opposed to *Neisseria gonorrhoeae*, by RLFP fragments as they would be obtained by applying the method of D4 in which the chromosomal DNA of the subtraction strain ("driver") is split by a restriction enzyme. This modification of the subtractive hybridization method described in D4 is not obvious.

- V) The claims against which objections have not been raised in the preceding paragraphs appear to be novel and to involve an inventive step.

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

PCT Article 6 stipulates that "The claim or claims shall define the matter for which protection is sought". In other words, the subject matter for which protection is sought is defined by the claim or claims *per se* and **not in the light of the description.**

- 1) Claims 1 to 5 and 11 to 13 do not satisfy the requirements of PCT Article 6, since the subject matter for which protection is sought is not clearly defined. The claims attempt to define this subject matter in terms of the result to be achieved. The technical features necessary to arrive at this result and to solve the problem are not present. It should also be noted that expressions of the type "comprise one or more sequences as they are found on" (claims 3 to 5) do not enable the DNAs to be characterized, since the sequence(s) in question may be very short (consisting of only 2 or 3 bases for example).

Furthermore, the feature "capable of hybridizing" is not a clear and acceptable technical feature, since the scope of the protection granted thereby varies depending on the hybridization conditions (claims 3 to 10, 12 and 13).

- 2) Although the expression "reading frame" forms part of the vocabulary of a person skilled in the art, the expression "with their reading frame" (in the context of claim 1) is unclear. By definition, any gene coding for a protein comprises a reading frame.

## VIII. Certain observations on the international application

Should it be understood that this expression implies that the genes in question are coding for proteins? If this is the case, why is the wording not clear and explicit? If this is not the case, the wording is obscure.

- 3) The terms:
- "part" (claims 1, 6 to 10, 15, 19, 21, 22)
  - "fragment" (claims 6 to 10, 18, 19, 20, 23)
- are not acceptable (PCT Article 6), since they are vague and ambiguous, which gives rise to uncertainty as to the real subject matter of these claims. Within said claims, these terms introduce nucleotide or polypeptide sequences which may be very small in size (for example, a codon having no technical relationship with the invention) and therefore easily debatable from the point of view of their novelty and/or inventive step. Consequently, these claims do not satisfy the requirements of PCT Article 6.
- 4) Expressions of the kind "*Neisseria meningitidis*-specific genes" (claim 18) or "*Neisseria meningitidis*-specific DNAs" (claim 24) lack clarity, since a specific feature is, in principle, defined in relation to a reference system.
- 5) In addition to its lack of clarity (see paragraph 4), claim 24 does not contain the technical features enabling (if this is in fact the aim sought) banks to be obtained containing the genes to be found in *Neisseria meningitidis* but not in *Neisseria gonorrhoeae* or *Neisseria lactamica* (a bank specific

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to *Neisseria meningitidis* as opposed to *Neisseria gonorrhoeae* or *Neisseria lactamica*). The claim does not therefore meet the requirements of PCT Article 6 in combination with PCT Rule 6.3(b), which specify that an independent claim must contain all the technical features necessary to define the invention.